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Preoperative chemo-radiotherapy (CHRT) in esophageal carcinoma (EC): response, toxicity and survival analysis

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Purpose: To evaluate preoperative ChRT in resectable localized EC. Patients (pts) treated with this combined modality in our institution were retrospectively reviewed.

Patients and Methods: From Jan 93 to Aug 98, 33 pts were treated, 32 M/1 F. Mean age 53 y (range 38–69). PS <= 1. Squamous cell: 32, adenocarcinoma 1. All of them were thoracic cancers: 3 upper 3rd, 24 middle 3rd and 6 distal 3rd. Preoperative work-up consisted of esophagoscopy, barium swallow, bronchoscopy, thoraco-abdominal CT scan and pulmonary function. Mean tumour length: 6.8 cm (range 5–12). N0: 25, N1: 8. Treatment protocol: two courses of CDDP 100 mg/m^2 d1 and 5FU 1000 mg/m^2 d1–5 on 1st and 6th wks, with radiotherapy (35 Gy) from 2nd to 5th wks, followed by esophagectomy on 10th wk.

Results: Thirty pts (91%) received full-projected preoperative treatment; 2 pts only one cycle of QT, and one pt 30 Gy. ChRT toxicity: 1 episode (ep) of neutropenia gr 3–4; 1 ep. thrombopenia gr 3–4; 11 ep. emesis gr 2 and 1 ep. gr 3; 3 ep mucositis gr 2–3. Twenty-seven pts (82%) were operated, 25 (76%) with curative resections. Two pts of 27 (7.5%) died of surgical complications. There were 6/33 (18%) pathological complete responses with ChRT and 21/33 (64%) partial responses. Median survival for all pts was 13 months and 3 years survival 25%. Median actuarial disease free survival was 13 months.

Conclusions: Preoperative ChRT is a well tolerated treatment. Pathological responses are seen frequently and surgical morbi-mortality is comparable to other series without preoperative approach. ChRT may improve prognosis of these pts by controlling local and distant disease, previous to definitive treatment. Marginally operable tumours may be resected in responding pts.

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Postoperative radiotherapy for gastric cancer

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Purpose: Surgery is considered as a primary treatment for locally advanced gastric cancer (LAGC). To improve local control and survival postoperative radiotherapy (RT) is investigated.

Methods: From 1986 to 1995 85 LAGC consecutive pts. were irradiated using high energy photons after resection, of whom D2 lymphadenectomy was performed in 10.5%, D1 in 76.5%, D0 in 13% of pts. Age: 30–77 yrs, mean-55 yrs, women: 26, men: 59. In 61 pts. RT was as adjuvant modality (R0 resection in pT3/T4 or pN1/N2 lesions), in 24 pts. it was given after R1 resection. No chemotherapy was given pre- or postoperatiely. RT to total dose of 46–60 Gy (median: 50.6 Gy) in 1.8–2.0 Gy per fraction was delivered.

Results: RT was well tolerated with no more than G2 acute toxicity according to RTOG/EORTC. The 5-yr overall actuarial survival (OS) rate was 37.5% (median survival: 21 mo). The disease-free survival rate (DFS) was 27.8% (median DFS: 16 mo). Independent survival related prognostic factors established using Cox multivariate analysis appeared to be: pT and pN. Neither presence of microscopic residual disease (R1 resection) nor the type of lymph node dissection (D) did show prognostic influence on survival after RT. The subset analysis showed best overall survival rates (OS-79% at 5-year) for pts. with pN0, independent from pT status. Combination of the worst prognostic factors: pT3/T4 and pN+ lead to survival rate of only 8%. Also for DFS – pN was the most important prognostic factor.

Conclusion: Postoperative external beam RT for LAGC does not influence OS and DFS in pts. treated primarily with non-optimal surgery (R0, R1 resection, D0, D1 lymphadenectomy). The potential benefit of RT may exist only for pN0 pts. after R1 resection, who cannot be reoperated.

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Taxotere–5FU Leucovorin (TFL) in advanced gastric carcinoma: A HeCOG phase II study

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Purpose: Taxotere has shown significant activity in advanced gastric carcinoma (as single agent RR: 23% and in combination with cisplatin RR: 58%). The purpose of this study was to assess the efficacy and toxicity of the TFL combination as first line chemotherapy in patients with advanced gastric carcinoma.

Methods: From Jan 1997 to Jan 1999 27 previously untreated parients (11 female and 18 male) with a median age of 63 (37 ± 76) and performance status 1 (0 ± 2) were enrolled. The site of metastatic disease was: locoregional (15 pts), liver (14 pts), lymph-nodes (5 pts), ascites (3 pts), lung (2 pts) and bones (1 pts). Chemotherapy consisted of Docetaxel (75 mg/m^2), 5 FU (500 mg/m^2) and Leucovorin (300 mg/m^2) on day 1 every 3 weeks.

Results: So far 104 cycles of chemotherapy were administered and up to now 25 patients were evaluated for toxicity and 19 for response. Objective responses were noted in 5 (26%) patients (1 CR, 4 PR), stable disease in 9 (48%) patients and progressive disease in 5 (26%) patients. Median duration of response was 10.4 (1.7 ± 11.77) months. Grade 3 and 4 toxicity was: neutropenia 31% of pts (but only 1 case of febrile neutropenia), thrombopenia 3.5% of pts, diarrea 10% of pts and mucocitis 3.5% of pts. There was one toxic death (febrile neutropenia).

Conclusion: TFL combination is an active regimen in patients with advanced gastric carcinoma, with acceptable toxicity. The median survival of the patients was comparable to established regimens.

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Modified ECF in the treatment of advanced oesophago-gastric cancer – An active regimen without the need for central venous catheter mediated therapy

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Introduction: ECF with prolonged infusional 5FU is an established active regimen for the treatment of advanced oesophago-gastric cancer. This treatment requires therapy through a central venous catheter. We reviewed our experience of a modified ECF regimen ("ECbolusF") for use in patients (pts) who refused continuous infusional therapy or who were considered unsuitable for such treatment.

Methods: A retrospective review of all pts with advanced oesophago-gastric cancer (24 oesophageal, 16 gastric, and 6 gastro-oesophageal) treated with ECbolusF between 6/94 and 6/98 was undertaken. 46 pts (34 male), median age 67 years (range 36–80) were treated with epirubicin 50 mg/m^2, cisplatin 60 mg/m^2, and 5-FU administered as a 6-hour infusion (bolus F) 600 mg/m^2 q 21 days. 26 pts had metastatic disease and 20 locally advanced disease at treatment commencement. The median number of cycles administered was 3 (range 1–9).

Results: 34 pts were evaluable for response and the overall response rate was 38%. A further 5 (15%) pts demonstrated stable disease. The median survival of all treated pts was 4.6 months. However, the median survival of the 37 pts who received at least 2 cycles of therapy was 6.9 months. ECbolusF was well tolerated with the only grade 4 toxicity recorded being diarrhoea (1 pt), and grade 3 toxicity of alopecia (9 pts), anaemia (2 pts), leucopenia (2 pts), and diarrhoea (1 pt). There were no treatment related deaths.

Conclusion: ECbolusF has demonstrated significant activity and was well tolerated in a patient group with biases that favoured a poor outcome. Evaluation of chemotherapy regimens that obviate the need for central venous catheter mediated therapy in advanced gastro-oesophageal cancer are recommended.

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Taxotere (T) in advanced solid tumors (AST) other than advanced breast cancer resistant to chemotherapy (CH) or hormonotherapy (H)

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Introduction: Patients (pts) with advanced disease resistant to previous CH or H were treated with T as single agent and evaluable for response (R)